

**Impact of adjuvant treatment modalities in breast cancer women  
who underwent modified radical mastectomy versus Breast  
conserving surgery on health related quality of life**

**Thesis Submitted in the partial fulfillment of  
Master degree in clinical Oncology**

**By**

**Mohamed Ramadan Gaber**

Bachelor of Medicine and Surgery, Alexandria University, Egypt.

Resident of clinical oncology

Mataria Teaching Hospital, Ministry Of Health

Under supervision of

**Prof. Mona Ahmed Aboul Enien**

Kasr Al-Ainy Center of Clinical Oncology and Nuclear Medicine

Faculty of Medicine, Cairo University

**Dr. Noha Yahia Abdu Ibrahim**

Assistant Professor of Clinical Oncology

Faculty of Medicine- Cairo University

**Dr. Wael Samir Makar**

Assistant Professor of Clinical Oncology

Faculty of Medicine- Cairo University

**Faculty of Medicine**

**Cairo University**

**2015**

# اثر طرق العلاج المختلفة لمرضى سرطان الثدي الذين خضعوا للإستئصال الجذري مقابل الجراحة التحفظية للثدي على الجودة الصحية لهؤلاء المرضى .

رسالة مقدمة من  
الباحث / محمد رمضان جابر  
بكالوريوس الطب والجراحة، -جامعة الاسكندرية  
طبيب مقيم علاج أورام  
مستشفى المطرية التعليمية

توطئة للحصول على درجة الماجستير فى علاج الأورام

لجنة الاشراف

ا.د. منى أحمد أبو العينين  
أستاذ علاج الأورام  
كلية الطب  
جامعة القاهرة

ا.م.د. وائل سمير مقار  
استاذ مساعد علاج الأورام  
كلية الطب – جامعة القاهرة

ا.م.د. نهى يحيى عبده إبراهيم  
أستاذ مساعد علاج الأورام  
كلية الطب- جامعة القاهرة

كلية طب القصر العينى  
جامعة القاهرة

٢٠١٥

## Acknowledgment

- ◎ *First, thanks are all due to Allah for Blessing this work until it has reached its end, as a part of his generous help throughout our life.*
- ◎ I would like to express my deepest gratitude and highest appreciation to *Prof.Dr. Mona Ahmed Aboul Enien*, Professor of clinical oncology, faculty of medicine, Cairo University, for her continuous encouragement, generous support and unlimited help, no word can express my gratitude.
- ◎ I would like to express my sincere gratitude to *Dr. Noha Yahia Abdu Ibrahim* , Assistant Professor of clinical oncology, faculty of medicine, *Cairo University*, who supervised this work with great interest and who gave me unlimited support throughout the work.
- ◎ Many thanks to *Dr. Wael Samir Makar*, Assistant Professor of clinical oncology, faculty of medicine, *Cairo University*,,for his continuous help, valuable suggestions, guidance and encouragement during the progress of this work.
- ◎ I wish to express my gratitude and special thanks to all my colleagues for their help and support.
- ◎ *I would like to express my extreme gratitude to all my professors, staff members and colleagues in Kasr El Einy center of oncology and nuclear medicine for their help and support.*
- ◎ Finally, No words can express my deepest appreciation and gratitude to *my family and my Wife Mrs. Amira samir* for their never ending support and care.

***Mohamed***

# **Table of Content**

<b>list of figures</b>	
<b>list of tables</b>	
<b>List of abbreviations</b>	
<b>Introduction and aim of work</b>	
<b>Review of literature</b>	
Chapter 1 : breast cancer diagnosis and management	
A. Incidence and Epidemiology of breast cancer	
B. Risk Factors and Diagnosis of breast cancer	
C. Different treatment modalities with their complications and side effects on breast cancer survivors	
D. Late and long term effects of treatment	
E. Follow up and long term implication of breast cancer survivors	
Chapter 2: Health Related Quality Of Life in breast cancer survivors.	
<b>Patients and methods</b>	
<b>Results</b>	
<b>Discussions</b>	
<b>Conclusion and recommendation</b>	
<b>References</b>	
<b>Arabic summary</b>	

## List of tables

<b>number</b>	<b>Title</b>	<b>page</b>
<b>Table 1</b>	<b>Surrogate definitions of intrinsic subtypes of breast cancer according to the 2013 St Gallen Consensus Conference.</b>	
<b>Table 2</b>	<b>Disease stage should be assessed according to the TNM system</b>	
<b>Table 3</b>	<b>Stage grouping system for carcinoma of the breast</b>	
<b>Table 4</b>	<b>demographic Characteristics of the study population N=172</b>	
<b>Table-5</b>	<b>profile of Mean score of all items in QLQ-C30 and QLQ-BR23 (N = 172):</b>	
<b>Table 6</b>	<b>Comparison of surgical treatment alternatives based on QOL scale scores.</b>	
<b>Table 7</b>	<b>Final linear regression model with parameter estimates for QLQ functional scales</b>	

## **List of figures**

<b>number</b>	<b>Title</b>	<b>page</b>
Figure 1	Factors with Significance association with QOL scale GHS mean scores	
Figure 2	Factors with Significance association with QOL scale physical function mean scores	
Figure 3:	Factors with Significance association with QOL scale Role function mean scores	
Figure 4:	Factors with Significance association with QOL scale emotional function mean scores	
Figure 5:	Factors with Significance association with QOL scale pain mean scores	
Figure 6:	Factors with Significance association with QOL scale fatigue mean scores	
Figure7:	Factors with Significance association with QOL scale sleep disturbance and appetite loss mean scores	
Figure8:	Factors with Significance association with QOL scale sexual enjoyment mean scores	
Figure9:	Factors with Significance association with QOL scale body image mean scores	
Figure10:	Factors with Significance association with QOL scale arm symptoms mean scores	

## **Abbreviations**

<b>QOL</b>	quality of life.
<b>HRQOL</b>	health related quality of life.
<b>EORTC</b>	European Organisation for Research and Treatment of Cancer
<b>C30</b>	core module composed of 30 questions
<b>BR23</b>	breast cancer specific module composed of 23 questions
<b>QLQ</b>	quality of life questionnaire.
<b>MRM</b>	modified radical mastectomy.
<b>BCS</b>	breast conservative surgery.
<b>ET</b>	endocrine therapy
<b>RT</b>	Radiotherapy.
<b>GHS</b>	Global health status

## **Health related quality of life (HRQOL): Impact of surgery and treatment modality in breast cancer**

**Mona A Aboul Enien<sup>1</sup>, Noha Y Ibrahim<sup>1</sup>, Wael S Makar<sup>1</sup>, Mohamed R Gaber<sup>2</sup>**

1 Clinical Oncology Department (NEMROCK), Kasr Al-Ainy School of Medicine, Cairo University, Egypt. 2 Clinical Oncology, Mataria Teaching Hospital, Egypt.

### **Abstract**

**Background:** Breast cancer is the most common malignancy among women leading to serious sequelae on the HRQOL. This was not well studied before in Egypt although it is the most important issue after survival.

### **Material and methods:**

This is a cross sectional study. The Arabic version of EORTC QLQ-C30 (version 3) and EORTC QLQ BR 23 questionnaire was administered to a random sample of 172 Egyptian women with breast cancer. There were 119 patients subjected to Modified radical mastectomy (MRM) and 53 to breast conservative surgery (BCS). Relevant descriptive statistics were computed for all items. The equality of means across the categories of each categorical independent variable was tested using parametric tests (ANOVA and independent t-test) or non-parametric tests (Kruskal Wallis and Mann Whitney tests) of association where appropriate.

### **Results:**

The mean age was 50.32 years ( $\pm$  SD 8.54) with a mean period of 4.75 years ( $\pm$  SD 3.33) from surgery. The global health was poor ( $28.38 \pm 11.7$ , 95% CI 30.71). Among the functional scales of QLQ-C30, social functioning scored the highest ( $87.91 \pm 17.92$ , 95% CI 91.64) whereas emotional functioning scored the lowest ( $59.61 \pm 24.96$ , 95% CI 64.66). The most distressing symptom on the symptom scales of QLQ-C30 was financial impact with a Mean of  $57.87 \pm 20.98$  (95% CI 62.24) Followed by fatigue  $39.43 \pm 17.70$  (95% CI 43.12) and pain  $36.44 \pm 18.07$  (95% CI 40.21). Using the disease specific tool it was found that body image and sexual functioning scored the lowest (Mean  $74.51 \pm 13.21$  &  $74.45 \pm 14.89$ , 95% CI 77.27 & 77.55) respectively. On the symptom scale, arm symptoms scored the highest with a mean of  $32.35 \pm 23.22$  (95% CI 37.19).

MRM patients had more favorable global health status and body image among the functional scale ( $p$ : 0.011, 0.027) due to social and religious issues. The functional scale was better in BCS with significant role function ( $p$ : 0.004). In the symptom scale, fatigue, pain, systemic side effects and arm symptoms were statistically significant better in the BCS ( $p$ : 0.004, 0.006, 0.002, and 0.003 respectively). Elderly illiterate postmenopausal patients with advanced stage, and lymphedema had more unfavorable HRQOL.

**Conclusion:** Egyptian breast cancer survivors reported lower overall global quality of life. HRQOL is better in BCS in spite of good global health and body image in MRM which related to social, demographic and religious issues. The quality of life should be integrated in the strategy of the treatment plan.

**Keywords:** breast cancer, quality of life, surgery





# **Introduction and aim of work**

# **Introduction**

A cancer diagnosis has tremendous consequences for most persons who experience it and breast cancer is the commonest malignancy among women and represents a global public health issue as it is one of the leading causes of cancer death among women around the world. <sup>(Groot MT et al (2006)</sup>

The first step in combating cancer is making the diagnosis. This requires a combination of careful clinical evaluation and diagnostic tests, which may include imaging, histopathology, cytology, and laboratory tests. <sup>(3)</sup> Once the diagnosis is confirmed, the cancer is staged, decision on therapy is made and an experimental systemic treatment protocol established. <sup>(4)</sup> For the majority of patients diagnosed with early stage breast cancer, the options for local treatment are mastectomy or breast conservative surgery with radiotherapy. <sup>(5)</sup>

The objectives of breast cancer treatment are eradication of the cancer, prolongation of life and quality of life improvement. The diagnosis of breast cancer and its subsequent treatment have been shown to have a significant influence on a woman's physical functioning, mental health, and well-being, causing substantial disruption to her Quality Of Life (QOL). <sup>(6- Broeckel JA, et al 2000)</sup>

Mortality rates of breast cancer are slightly decreasing due to early diagnosis and improvements in treatment. Since standard radical mastectomy was established first by Halsted for breast cancer surgery, the extent of surgical intervention gradually decreased with the results of numerous randomized controlled trials. <sup>(7- Harris JR et al, 2000)</sup> Although Breast Conservative Surgery (BCS) is said to have a better effect on body image and sexual activity, Modified Radical Mastectomy (MRM) is preferred by both patients and surgeons yet it has not been proven to affect survival any more than BCS, and with increasing life time expectancy and less extensive surgical procedures, quality of life concept gained importance and popularity. <sup>(8- Poggi MM et al, 2003)</sup>

Cancer survivors are at increased risk for co-morbid conditions <sup>(9- Demark-Wahnefried W et al 2005)</sup> and have reported a poor or fair health, psychological disability, limitations in daily life and reduced ability to work after breast cancer compared to the general population. <sup>(10- Hewitt M et al 2003)</sup>

Despite these problems, less medical care has been documented for cancer survivors compared to patients without a cancer history. <sup>(11-Earle CC et al, 2004)</sup>

For survivors of breast cancer, problems include higher co morbidity and mortality that have been related to some breast cancer regimens, <sup>(12)</sup> functional impairment and poorer economic outcomes. <sup>(13-Chirikos TN, et al 2002)</sup>

Among the quality of life studies in cancer patients, breast cancer has received most attention for several reasons. First, the number of women with breast cancer is increasing. It has been reported that each year over 1.1 million women worldwide are diagnosed with breast cancer and 410,000 die from the disease <sup>(14- Stewart BW,et al ,2003)</sup> Secondly, early detection and treatment of breast cancer have improved and survivors now live longer, so studying quality of life in this context is important. Thirdly, breast cancer affects women's identities and therefore studying quality of life for those who lose their breasts is vital. In addition, it is believed that females play important roles as partners, wives, and mothers within any family. Thus, when a woman develops breast cancer, all members of family might develop some sort of illnesses. In fact, breast cancer is a family disease. Other reasons could be added, but overall it is crucial to recognize that with increasing improvements in medicine and medical practice during recent years studying quality of life for any cancer, for any anatomical site and for either gender is considered highly relevant. <sup>(15- Mandelblatt J,et al ,2004)</sup>

Health-related quality of life is now considered an important endpoint in cancer clinical trials. It has been shown that assessing quality of life in cancer patients could contribute to improved treatment and could even be as prognostic as medical factors could be prognostic. <sup>(16- Montazeri A,et al, 1996)</sup>

Evaluation of Health-Related Quality Of Life (HRQOL) is important in chronic diseases; it is a better indicator of patients' function and well-being compared to the physicians' clinical and Para-clinical indices. HRQOL is important in the field of oncology since, according to recent advancements, patient survival is no longer the sole issue and according to the recent studies, HRQOL is now second only to survival. <sup>(17- Shimozuma K,et al 2007)</sup>

HRQL can be defined as self-perceived aspects of wellbeing that are related to or affected by the presence of a disease or treatment <sup>(18-Ebrahim S,et al, 1995)</sup> As a multidimensional construct, it includes perceptions, both positive and negative, of several dimensions such as physical, emotional, social and cognitive functioning.

It also includes the negative aspects of somatic sensation disorders and symptoms caused by a disease and/or its treatment.

Studies undertaken in different settings or in different countries might display slight divergences, as HRQL is also modulated by cultural and care patterns. (19-Osoba D, et al. 1994)

Measuring quality of life in breast cancer patients has been the focus of clinical practice and research in recent decades and is of importance in assessing treatment outcomes (20-Perry SH, et al, 2007) (21-Grimison P, et al, 2007)

Thus the issue of 'survivorship' now has become an important topic in breast cancer care that demands the investigation of long term effects of breast cancer diagnosis and its treatments (22-Mols F, et al, 2005)

The time of diagnosis, initial stages of adjuvant treatment course and the months immediately following the end of adjuvant treatment are transition times of poor adjustment and decreased quality of life in breast cancer patients. (23-Frost MH, et al, 2000)(24-Schnipper HH et al 2001)

Emphasizing that at least 25 to 35% of patients experience psychological disorders differing gradually from anxiety to major depression and sexual function disorders which continue minimum two years despite treatment. (25-Ries L, et al, 1999)

During the last decades several questionnaires to assess QOL have been developed. In breast cancer one of the most frequently used questionnaires to measure health-related quality of life is the Quality of Life Questionnaire Core module with 30 items (EORTC QLQ-C30) and its breast-cancer-specific module (EORTC-BR23) provided by the European Organization for Research and Treatment of Cancer. (28-Erickson P, et al 2011)

The QLQ-C30 is a multi-dimensional assessment tool as it includes a range of items covering physical, emotional and social health issues being relevant to cancer patients irrespective of diagnosis. (26-Aaronson NK, et al, 1993) It can be used for detection of early and long-term consequences of the cancer disease itself and its treatment. Further, the QLQ-C30 can be used for individual patient management as well as for evaluation of undesired treatment effects on the group level. There is sufficient evidence to support its reliability and validity. (27-Fayers PM, et al, 2001)

Once active treatment is completed, some women celebrate; others become anxious about recurrence and feel that they have lost a proactive shield against cancer. (29-Casso D, et al, 2004)

Many studies report persistent disturbances in family functioning because marital issues were ignored during the cancer treatment phase. Body image and age, especially after mastectomy, have also been detected as concerns. (30-Vacek PM, et al, 2003) (31-Remennick L., et al, 2006)

Very little researches have compared the HRQOL of women treated with modified radical mastectomy (MRM), with the HRQOL of women experiencing breast conservative surgery BCS. Factors such as patient education, spouse support and, financial stability, and disease stage, have been found to influence not only quantity of survival, but also HRQOL.

**In 2009 a Turkish study** investigated 74 breast cancer patients whose follow-up exceeds minimum 12 months from diagnosis without any recurrence and distant metastasis. Results showed that Quality of life after BCS was found better than MRM so they recommended that breast conserving surgery will positively affect not only the patients but also the people who were living with them. <sup>(33-Zanapalioglu et al, 2009)</sup>

**In 2009 a Mexican study** aimed to identify and examine the effects of cancer stage and surgical treatment on the quality of life (QOL) of Mexican women with early stage breast cancer treated with either modified radical mastectomy (MRM) or breast conservative surgery (BCS), plus adjuvant chemotherapy.

Results showed that MRM and BCS are essentially equivalent choices in terms of QOL, with the exception of the impact on body image. <sup>(34-Gómez-Rico JA, et al, 2009)</sup>

**In 2012 an Iranian study** selected 160 MRM patients and 127 BCS patients were examined and results showed that significant difference attributed to a significantly better body image in the BCS group compared to the MRM group. <sup>(35-Negin Hadi MD MPH, et al, 2012)</sup>

**In 2012 the Middle East Bahrain study** in which the Arabic version of the European Organization for Research and Treatment of Cancer general quality of life questionnaire (QLQ-C30) and the disease specific questionnaire (QLQ-BR23) were administered to a random sample of 337 Bahraini women with breast cancer.

Results showed that Participants had a mean score for global health of 63.9 (SD±21.3). Among functional scales, social functioning scored the highest mean (77.5) whereas emotional functioning scored the lowest (63.4). The most distressing symptom on the symptom scales of QLQ-C30 was fatigability (Mean 35.2). Using the disease specific tool (QLQ-BR23) it was found that sexual functioning scored the lowest mean (25.9) whereas "upset due to hair loss" symptom scored the highest mean (46.3). Significant mean differences for various functional and symptom scales were observed among categories of age, marital status, type of surgery, stage of disease, monthly income, educational status and time since diagnosis.

So Bahraini women showed good functioning on most functional and symptom scales; poorest functioning was reported for emotional and sexual domains. On the symptom scales, fatigue and arm morbidities were the most bothersome symptoms. <sup>(37- Jassim, et al, 2012)</sup>

**In 2014 another Turkish study** evaluates the changes in quality of life of the female patients who had undergone surgical treatment for breast cancer. A total of 250 female patients Results showed that Breast conserving surgery has a more favorable impact on general wellbeing, when the identical parameters were taken into consideration, relatively favorable outcomes of BCS on the patients were observed relative to mastectomized patients. Besides, though not statistically significant, BCS has more patient-friendly effects on sexual function and sexual satisfaction in comparison with mastectomy. Patients with advanced stage disease and elder patients had more unfavorable health related quality of life (HRQOL) scores than younger patients, and those in their early stages of breast cancer. <sup>(36-Mustafa Akça2,et al, 2014)</sup>

To enhance the QOL for women with breast cancer, more QOL studies are needed to investigate the effect of socio-demographic and clinical factors on their QOL. <sup>(32-Pandey M,et al, 2005)</sup>

We were able to locate few documents that surveyed HRQOL in women who underwent MRM or BCS in Egypt but we were unable to locate any documents that surveyed different factors beyond surgery that affect HRQOL or HRQOL in breast cancer survivors and its impact on society.

Therefore, The aim of this study is to assess the effect of demographic, medical factors and adjuvant treatment modalities (radiotherapy and/or chemotherapy and/or hormonal therapy) on the quality of life scales of the Egyptian women with breast cancer between the two groups of patients who underwent breast conserving surgery (BCS) and modified radical mastectomy (MRM) using EORTC QLQC30, and EORTC QLQ-BR23 questionnaire forms.

So we can identify and examine the relationship between different treatment modalities and HRQOL among breast cancer survivors.

We can also examine predictors of QOL so we can enable better decision making for both physicians and patients.